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(54) Bone replacement filler material

(23) Application No.: S58 – 46775
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(72) Inventor: Kazuo KONDO
c/o NGK Spark Plug Co., Ltd.
14 - 18 Takatsuji-cho, Mizuho-ku, Nagoya
(72) Inventor: Tatsunori KURACHI
c/o NGK Spark Plug Co., Ltd.
14 - 18 Takatsuji-cho, Mizuho-ku, Nagoya
(72) Inventor: Yuhi FUKUURA
c/o NGK Spark Plug Co., Ltd.
14 - 18 Takatsuji-cho, Mizuho-ku, Nagoya
(71) Applicant: NGK Spark Plug Co., Ltd.
14 - 18 Takatsuji-cho, Mizuho-ku, Nagoya

Specification

1. Title of the Invention

Bone replacement filler material

2. Range of Patent Claims

(1) A bone replacement filler material characterized by a spherical or polyhedral shape and made from sintered calcium phosphate for use as a bone replacement filler material in replacing portions of bone that are missing following the removal of a bone tumor.

(2) The bone replacement filler material described in patent Claim 1 having 1, 2 or more holes and/or protuberances in its spherical or polyhedral surface.

3. Detailed Description of Invention

This invention pertains to bone replacement filler material that fills in missing portions of bone in living organisms.

After removing a bone tumor or other anomalous cells from a living organism, it is considered best to use one's own bone to fill the resulting section of missing bone. When the space to fill is such that one's own bone cannot be used, donor bone, frozen bone or acrylic cement have been used as substitutes. However, frozen bone and donor bone are not only in limited supply, they have not yet been approved in Japan. There are no problems of supply with acrylic cement, but it has no affinity with living tissue. For such reasons, the use of sintered alumina as an artificial bone replacement has been studied, but this has not yet reached the stage of practical use owing to its poor adhesion to living tissue.

After examining the possibility of using various ceramics as a bone replacement material, the inventors discovered that sintered calcium phosphate not only caused no rejection reaction in living tissue, but it also had superior adhesion to living tissue. They also found that it can be worked into complex shapes.

This invention was made possible based on the aforementioned observations, and it provides a bone replacement filler material characterized by having holes and/or protuberances along its surfaces which can be either polyhedral or spherical and made from sintered calcium phosphate for use as bone replacement filler material to replace portions of bone that are missing following the removal of a bone tumor.

It is desirable to have the Ca/P atoms in the sintered calcium phosphate (A) used in the bone replacement filler material of this invention (hereafter abbreviated to "(A)") in a range of 1.4 ~ 1.75. Even more desirable is to have the sintered material (C) (hereafter abbreviated to "(C)") composed of (85 ~ 99.5 wt. % (A) and 0.5 ~ 15 wt. % of the frit (B) shown in the table (hereafter abbreviated to "(B)"). A sintered material made of 77 ~ 97 wt. % and 3 ~ 23 wt. % Y_2O_3 also works quite well. Each of these has been disclosed in Japanese Unexamined Patent S55 – 56062 "High-Strength Sintered Calcium Phosphate Manufacturing Method," Japanese Unexamined Patent S55 – 140756 "High-Strength Sintered Calcium Phosphate" and Japanese Unexamined Patent S55 – 80771 "High-Strength Sintered Calcium Phosphate" respectively.

	"Frit Component Ratios" (Mol %)								
Frit Name	P_2O_5	BaO	CaO	MgO	ZnO	Na_2O	K_2O	Al_2O_3	SiO_2
A	46	32	20					2	
B	46	47	---	7					
C	47	---	44		9				
D	60	20	5	5			5	5	
E	43	3	41	2		10			1
F	47	3	49					1	
G	70	10		10	5			5	

Each of the above sintered calcium phosphate samples has excellent affinity and adhesion with living tissue, but when they are used as a bone replacement filler material the shape is not necessarily limited to polyhedral and spherical shapes, so in order to improve both of the above characteristics even further and to prevent the shifting around of the filler material, it is possible to form multiple holes or protuberances in the surface while shaping them.

This invention is described with reference to the embodiments below.

Embodiment 1

Commercially available compounds of H_3PO_4, $BaCO_3$, $CaCO_3$, $MgCO_3$ and Al_2O_3 were mixed by weight to achieve the following composition following baking (mol standard) P_2O_5: 47%; BaO_2: 5%; CaO: 49.5% and Al_2O_3: 1.0%. This mixture was baked at a temperature of 1300 °C and maintained for 5 hours to put it in a molten state and the molten mixture was quenched, producing the frit 1. The frit 1 was pulverized using a Trommer device until the particles 5 μm or smaller constituted 40 wt. % and the frit powder thus obtained was mixed wet with a commercially available hydroxyapatite powder having an average granularity of 0.1 μm at a ratio of 5 wt. % to 95 wt. %, respectively, and then dried. As a binder, 3 wt. % camphor was added (in relation to 100 wt. % of the final, theoretical product) and, after drying, a sphere measuring 8 mm in diameter was produced using the rubber press method. Next, using an NC lathe, 12 1 mm X 2 mm holes were made in the surface of this sphere in positions symmetrical to the sphere. Then, it was baked for an hour at a temperature of 1200 °C, resulting in a spherical filler material that had holes in its surface. This filler material was implanted in the femur of a rabbit and removed 7 weeks later. When it was studied for possible harm to living tissue, there had been no foreign substance reaction and, bone formation at the periphery was observed, demonstrating that it was fulfilling its role as a filler material.

Embodiment 2

Commercially available compounds of $CaCO_3$ and H_3PO_4 were mixed by weight to achieve the following composition following baking: Ca / P_2O_5 mol ratio of 1.2. This mixture was baked at a temperature of 1300 °C and maintained for 2 hours to put it in a molten state and the molten mixture was quenched, producing the frit 2. The frit 2 was pulverized under the same conditions as Embodiment 1. The frit powder thus obtained was mixed wet with a commercially available tertiary calcium phosphate powder having an average granularity of 0.5 μm at a ratio of 6 wt. % to 85 wt. %. Commercially available Y_2O_3 was added to amount to 9 wt. % and the mixture was then dried. As a binder, 3 wt. % camphor was added (in relation to 100 wt. % of the final, theoretical product) and, after drying, a equilateral octahedron measuring 10 mm on a side was produced using the rubber press method. Then, it was baked for an hour at a temperature of 1200 °C, resulting in a regular, octahedral filler material. This octahedral filler material was implanted in the femur of a rabbit and it was found that it fulfilled its role as a filler material in the same way as Embodiment 1.

Embodiment 3

Frit powder having the same composition as the frit 2 obtained in Embodiment 2 was mixed with commercially available tertiary calcium phosphate powder having an average granularity of 0.5 μm at a ratio of 6 wt. % to 85 wt. % respectively. Commercially available Y_2O_3 was added to amount to 9 wt. % and to these powders was added 4 times as much water (by weight) which was used to create a turbid mixture. This was poured into a gypsum mold and after leaving it for one day, the mixture was baked at a temperature of 900 °C and kept at that temperature for one hour. The spherical filler material 1 measuring 8 mm in diameter having protuberances 2 like those shown the drawing was the result. When this filler material was implanted in the femur of a rabbit, it was found to fulfill the same role as the filler material in Embodiment 1.

As above, the filler material of this invention has superior affinity and adhesion with living tissue as well as superior shaping versatility, making it useful as a living tissue material.

Furthermore, the filler material in this invention can be formed by not only the rubber press forming method and the casting method disclosed in the embodiments, but also metal die press methods, injection forming methods and many other conventional forming methods.

And, in the embodiments, all of the implants were formed before baking, but for complex forms having both holes and protuberances in the surface, it would be desirable to work the objects further with a drill or lathe after baking. The sintered calcium phosphate constituting the filler material of this invention lends itself easily to forming processes of these sorts.

4. Simple Description of Drawing

The drawing shows a three dimensional rendering of one of the embodiments of the bone replacement filler material.

2: Protuberances

Patent Applicant: Shuji OGAWA, Representative [stamp]
NGK Spark Plug Co., Ltd.
14 - 18 Takatsuji-cho, Mizuho-ku, Nagoya

Procedure Correcting Document (Voluntary)
March 16, 1984

To: Kazuo WAKASUGI, Patent Office Official

1. Disclosure of Matter
   1983 Patent Application No. 46775

2. Title of the Invention
   Bone replacement filler material

3. Person Making Correction
   Relationship to the Matter: Patent Applicant
   Shuji OGAWA, Representative /stamp/
   NGK Spark Plug Co., Ltd.
   14 - 18 Takatsuji-cho, Mizuho-ku, Nagoya 454
   Tel.: (052) 264 – 4821
   Tokyo Contact No.: 440 - 6111

4. Matter to be Corrected
   Section(s) in the detailed description of the invention within the specification.

5. Content of Correction(s)
   As attached.

1. Line 6 on Page 7 of the Detailed Description /Translator's Note: Fragment in Embodiment 2./

The section "baked at a temperature of 1200 °C and maintained for 1 hour" shall be corrected to read "baked at a temperature of 1300 °C and maintained for 2 hours."

2. The section from line 1 to line 14 on page 8 of the aforementioned document shall be corrected to read as follows. /Translator's Note: The last line of Embodiment 3 to the simple description of the drawings./

"was found to fulfill the same role as the filler material in Embodiment 1.

Embodiment 4

A frit powder having the same composition as that in Embodiment 1 was wet-mixed with hydroxyapatite and dried. A plastic agent amounting to 2 wt. % and a resin amounting to 30 wt. % of the full amount (100 wt. %) of the final theoretical product was added to this and mixed and kneaded for two hours. A sphere measuring 5 mm in diameter having 1 mm X 2 mm protuberances in its surface was formed in a low-pressure injection molding device. Next, eight 1 mm X 1 mm holes were drilled using a drill and the sphere was baked at a temperature of 1300 °C and held for a period of one hour. This produced a spherical filler material that had both holes and protuberances. When this filler material was implanted in the femur of a rabbit, it was found to fulfill the same role as the filler material in Embodiment 1.

As above, the filler material of this invention has superior affinity and adhesion with living tissue as well as superior shaping versatility, making it useful as a living tissue material. Furthermore, the filler material in this invention can be formed by not only the rubber press forming method, the casting method and the low-pressure injection method disclosed in the embodiments, but also by metal die press methods, injection forming methods and many other conventional forming methods."

END

⑲ 日本国特許庁（JP）　　⑪ 特許出願公開

⑫ 公開特許公報（A）　　昭59—171546

⑤1Int. Cl.³	識別記号	庁内整理番号	④3公開　昭和59年(1984)9月28日
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発明の数　1
審査請求　未請求

（全 4 頁）

⑤4代替骨用充填材

⑦1出　願　人　日本特殊陶業株式会社
名古屋市瑞穂区高辻町14番18号

⑦2発　明　者　福浦雄飛
名古屋市瑞穂区高辻町14番18号
日本特殊陶業株式会社内

⑦2発　明　者　倉地辰則
名古屋市瑞穂区高辻町14番18号
日本特殊陶業株式会社内

⑦2発　明　者　近藤和夫
名古屋市瑞穂区高辻町14番18号
日本特殊陶業株式会社内

②1特　願　昭58—46775
②2出　願　昭58(1983)3月18日

明　細　書

1．発明の名称

代替骨用充填材

2．特許請求の範囲

(1) 骨腫瘍摘出後の骨欠損部に補充する代替骨用充填材において、燐酸カルシウム焼結体からなり、多面体形状又は球形状を有することを特徴とする代替骨用充填材。

(2) 多面体又は球の表面に一又は二以上の穴及び／又は突起を有する特許請求の範囲第1項記載の代替骨用充填材。

3．発明の詳細な説明

本発明は生体中の骨欠損部に補充する代替骨用充填材に関するものである。

骨腫瘍等の骨異常細胞を生体中から摘出した後に摘出部分に生じた骨欠損部に補充する代　骨としては、自家骨が最良とされ、自家骨では補充できない程に骨欠損部の容積が大きい場合には他人の骨、冷凍骨又はアクリルセメントが利用されていた。しかしながら、他人の骨及び冷凍骨はいずれもその数量に限界があるうえに、我国では認可されていない。又アクリルセメントは数量的に問題はないが、生体親和性が良くない。そこでアクリルセメントに代わる人工代替骨材としてアルミナ焼結体の利用研究がなされたが、アルミナは本質的に生体との密着性に劣っているために実用に至ってない。

発明者等は各種セラミックスの代替骨材としての利用可能性を検討した結果、燐酸カルシウム焼結体が生体との異物反応を生ぜしめず且つ密着性に優れ、更に複雑な形状に加工することができるものであることを見出したのである。

本発明は上記の知見に基づいて得られたもので、骨腫瘍摘出後の骨欠損部に補充する代替骨用充填材において、燐酸カルシウム焼結体からなり、多面体形状又は球形状又はこれらの表面に穴及び／又は突起を有する形状を有することを特徴とする代　骨用充填材を提供するものである。

本発明代　骨用充填材に使用する燐酸カルシウム焼結体としてはCa／P原子が1．4～1．75

の範囲にあるもの（A）（以下（A）と略称）が望ましく、更に望ましくは、（A）85～99.5重量%と表に示すフリット（B）（以下（B）と略称）0.5～15重量%からなる焼結体（C）（以下（C）と略称）及び（C）77～97重量%とY_2O_3 3～23重量%とからなる焼結体が好適であり、これらはそれぞれ特開昭55－56062号「高強度リン酸カルシウム焼結体の製造法」、特開昭55－140756号「高強度リン酸カルシウム焼結体」及び特開昭55－80771号「高強度リン酸カルシウム焼結体」に開示されている。

	[フリット成分割合] モル%								
フリット名	P_2O_5	BaO	CaO	MgO	ZnO	Na_2O	K_2O	Al_2O_3	SiO_2
A	46	32	20					2	
B	46	47	－	7					
C	47	－	44		9				
D	60	20	5	5			5	5	
E	43	3	41	2		10			1
F	47	3	49					1	
G	70	10		10	5			5	

上記各燐酸カルシウム焼結体はいづれも本質的に生体との親和性及び密着性に優れたものであるが、代替骨用充填材として使用する場合にはその形状は通常の多面体や球に限定されず、上記両特性を一層向上させることと充填材の移動防止とを目的として成形時に表面に複数の穴や突起を形成しても良い。

以下実施例により説明する。

実施例1

焼成後の組成がモル基準でP_2O_5 47%、BaO 2.5%、CaO 49.5%、Al_2O_3 1.0%となるように市販のH_3PO_4、$BaCO_3$、$CaCO_3$、$MgCO_3$、及びAl_2O_3を用いて秤量混合し、該混合物を温度1300℃、保持時間5時間の条件で焼成し溶融状態とし、溶融物を急水冷することによってフリット1を得た。フリット1をトロンメルにて5μm以下の粒子が40重量%に達するまで粉砕し、得られたフリット粉末5重量%と平均粒径0.1μmの市販水酸アパタイト粉末95重量%を湿式混合し乾燥し、バインダーとして最終理論生成物100重量%に対し3重量%のカンファーを添加混合し乾燥後、ラバープレス法により直径8mmの球を製作し、次いでNC旋盤を用いてこの球の表面の球対称位置に1$^{\phi}$×2mmの穴を12個穿設した後、温度1200℃、保持時間1時間の条件で焼成することによって表面に穴を有する球形充填材を製作した。この充填材を兎の大腿部に埋入し、7週間後に取り出して生体為害性を調べたところ、異物反応はなく、しかも周囲に骨形成が認められ、充填材としての役目を果たしていることがわかった。

実施例2

焼成後の組成がCa/P_2O_5モル比1.2となるように市販の$CaCO_3$及びH_3PO_4を用いて秤量混合し、該混合物を温度1300℃、保持時間2時間の条件で焼成し溶融状態とし、溶融物を急水冷することによってフリット2を得た。フリット2を実施例1と同一条件で粉砕し、得られたフリット粉末6重量%と平均粒径0.5μm

の市販燐酸三カルシウム粉末85重量%と市販Y_2O_3粉末9重量%とを湿式混合し乾燥し、バインダーとして最終理論生成物100重量%に対し3重量%のカンファーを添加混合し乾燥後、ラバープレス法により一辺長10㎜の正八面体を製作し、次いで温度1200℃、保持時間1時間の条件で焼成することによって正八面体形充填材を製作した。この充填材を兎の大腿部に埋入したところ、実施例1と同様に充填材の役目を果たしていた。

実施例3

実施例2で得たフリット2と同一組成のフリット粉末6重量%と平均粒径0.5μmの市販燐酸三カルシウム粉末85重量%と市販Y_2O_3粉末9重量%とをこれら全粉末の4倍重量の水を用いて湿式混合し泥漿とし、石膏型に流し込み、1日放置後、温度900℃、保持時間1時間の条件で焼成することによって図に示す如く表面に突起2を有する直径8㎜の球形充填材1を製造した。この充填材を兎の大腿部に埋入したところ、実施例1と同様に充填材の役目を果たしていた。

以上のように本発明充填材は、生体親和性、密着性及び加工性に優れているので、生体材料として有用である。

尚、本発明充填材は、実施例で示したラバープレス成形法、鋳込み成形法のみならず、金型プレス成形法、射出成形法等各種従来成形法によって成形することができる。

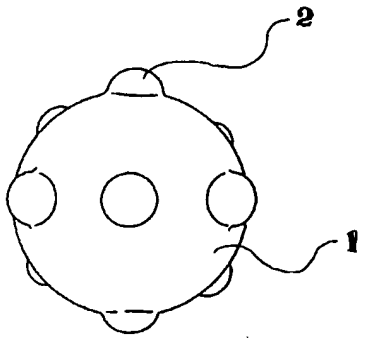
また、実施例ではいずれも焼成前に成形したが、表面に穴と突起の両方を有するような複雑な形状のものについては焼成後に旋盤加工やドリル加工によって加工するのが望ましく、本発明充填材を構成する燐酸カルシウム焼結体はこのような成形加工をも容易に成さしめるものである。

4．図面の簡単な説明

図面は本発明代替骨用充填材の一実施例を示す立体図である。

2……突起

特許出願人　日本特殊陶業株式会社
代表者　小川　修次



手　続　補　正　書（自発）

昭和59年3月16日

特許庁長官　若　杉　和　夫　殿

1. 事件の表示
昭和58年特許願　第46775号

2. 発明の名称
代替骨用充填材

3. 補正をする者
事件との関係　特許出願人
〒467-91
名古屋市瑞穂区高辻町14番18号
(454)日本特殊陶業株式会社
代表者　小　川　修　次
（電話 <052> 264-4821）
（連絡先 東京営業所 440-6111）

4. 補正の対象
明細書中、発明の詳細な説明の欄。

5. 補正の内容
別紙の通り

1 明細書第7頁第6行目、

「作し、次いで温度1200℃、保持時間1時間の」を「作し、次いで温度1300℃、保持時間2時間の」に訂正します。

2 同第8頁第1行目から同第14行目までを下記の通り訂正します。

「1と同様に充填材の役目を果たしていた。

実施例4

実施例1と同一組成のフリット粉末と水酸アパタイト粉末を湿式混合し乾燥し、最終理論生成物100重量%に対し30重量%の樹脂および2重量%の可塑剤を入れ、2時間混練し、低圧の射出成形にて表面に1φ×2㎜の突起を6個有する直径5㎜の球を成形し、次いでドリル加工にて1φ×1㎜の穴を8個穿設した後、温度1300℃、保持時間1時間の条件で焼成することにより、表面に突起および穴を有する球形充填材を製作した。この充填材を兎の大腿部に埋入したところ、実施例1と充填材の役目を果たしていた。

以上のように本発明充填材は生体親和性、密着性および加工性に優れているので生体材料として有用である。なお、本発明充填材は実施例で示したラバープレス成形法、鋳込み成形法、低圧射出成形法のみならず、金型プレス成形法等各種従来成形法によって成形することができる。」

以　上